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Homology of the TetM with translational elongation factors: implications for potential modes of tetM conferred tetracycline resistance

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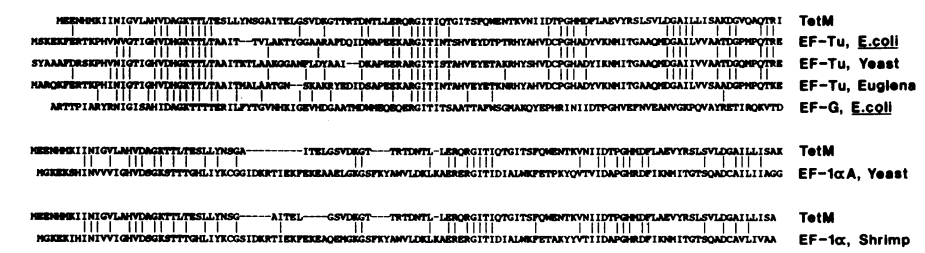
After our determination of the nucleotide sequence of tetM isolated from Ureaplasma urealyticum (1), we searched by computer analysis for homology of the amino acid sequence coded by the largest open reading frame of our nucleotide sequence and the tetM gene reported from Streptococcus pneumoniae (2) against sequences in pDayhoff. The analysis revealed that the N-terminal region of TetM shares a significant degree of homology with the N-terminus of five diverse translational elongation factors. These observations suggest potential roles for TetM in the modulation of tetracycline sensitive cellular events.

Although most of the known tetracycline resistance genes found in bacteria code for products involved in the active efflux of the antibiotic, the tetM determinant codes for a gene product that apparently binds to ribosomes conferring tetracycline resistance to them both in vivo and in vitro (3). It seems reasonable to propose that the homologous regions between the resistance factor and elongation factors constitute their respective ribosome binding sites. Recent evidence indicates that tetracycline binds to the S7 protein of the 30S subunit of the ribosome (4). This event could presumably preclude the binding of aminoacyl-tRNA to the ribosome acceptor site thus blocking translation. As a result, two potential mechanisms by which the TetM acts are suggested. 1) The tetM gene product could bind to the ribosome preventing tetracycline binding to the S7 protein but permitting productive binding of the aminoacyl-tRNA. Whether or not tetracycline can bind or is bound to the ribosome in the presence of the tetM product remains to be determined. Alternatively, 2) TetM could act as a tetracycline resistant elongation factor. In this mode, the aminoacyl-tRNA could bind productively to the ribosome regardless of or in addition to tetracycline binding.



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